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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/698,541	10/30/2003	Jennifer M. Burns	019934-003360US	9963

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EXAMINER	
HAMUD, FOZIA M	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 06/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/698,541	BURNS ET AL.	
	Examiner	Art Unit	
	Fozia M. Hamud	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-38* is/are pending in the application.

4a) Of the above claim(s) *11-27 and 33-38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10 and 28-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/19/04; 5/19/04;* 02/28/05,
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Office Action

Election/Restrictions:

1a. Applicants' election with traverse of Group I, (claims 1-10 and 28-32), filed on 30 May 2006 is acknowledged.

Applicant's ground of traversal is that according to the MPEP, where claims can be examined together without undue burden, the Examiner must examine the claims on the merits even though they are directed to independent and distinct inventions. In establishing that an "undue burden" would exist for co-examination of claims, the Examiner must show that examination of the claims would involve substantially different prior art searches, making the co-examination burdensome. Applicants respectfully submit that examination of the claims in Groups I-IV would not create an undue burden and respectfully request withdrawal of the restriction.

Applicant's traversal has been fully considered but is not deemed persuasive. The inventions of Groups I-IV have a separate status in the art as shown by their different classifications. As such, it would be burdensome to search the inventions of the instant Groups together.

The restriction requirement is still deemed proper and is therefore made FINAL.

Status of Claims:

1b. Claims 1-38 are pending, of which claims 1-10 and 28-32 are drawn to the elected invention, and will be searched and examined. Claims 11-27 and 33-38 are withdrawn from consideration by the Examiner as they are drawn to non-elected invention.

Specification:

2a. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code, on page 20, lines 20-21. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Information Disclosure Statement

3. The information disclosure statements (IDS) submitted on 19 March 2204, 19 May 2004, 28 February 2005, 08 August 2005 and 09 January 2006 have been received and comply with the provisions of 37 CFR §1.97 and §1.98. The references have been placed in the application file and the information referred to therein has been considered as to the merits.

Claim rejections-35 USC § 112, First Paragraph:

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-10 and 28-32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of identifying an agent that binds to the CCX-CKR2 of SEQ ID NO:2, by contacting a plurality of agents to said polypeptide and selecting an agent that competes with I-TAC OR SDF1 for binding to the said CCX-CKR2 polypeptide, does not reasonably provide enablement for a method of identifying an agent that binds to the CCX-CKR2 of SEQ ID NO:2, by contacting a plurality of agents to a CCX-CKR2 polypeptide comprising 95% to SEQ ID NO:2, or a

fragment of SEQ ID NO:2, or a fragment of SDF1 or I-TAC, and selecting an agent that competes with I-TAC or SDF1 for binding to the said CCX-CKR2 polypeptide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, practice the invention commensurate in scope with these claims.

Claims 1 and 28 encompass using a CCX-CKR2 polypeptide which comprises 95% identity to SEQ ID NO:2, or a fragment of SEQ ID NO:2, or a fragment of SDF1 or I-TAC to identify an agent that binds to CCX-CKR2. The specification describes CCX-CKR2 polypeptide as comprising the amino acid sequence set forth in SEQ ID NO: 2, 4, 6, 8 or 10. Since the specification does not teach what the differences are between these sequences, it is interpreted for the record that CCX-CKR2 polypeptide comprises the amino acid sequence of SEQ ID NO:2. It is also understood that CCX-CKR2 of SEQ ID NO:2 is used in the methods disclosed in this application, unless Applicant contends otherwise. The specification discloses that CCX-CKR2 polypeptide binds to radiolabeled SDF1 and I-TAC and that said binding is competed by cold competitors SDF1 and I-TAC, (see page 51, lines 10-14). However, the specification does not demonstrate that a fragment of CCX-CKR2 polypeptide of SEQ ID NO:2 or a CCX-CKR2 polypeptide that comprises 95% identity to SEQ ID NO:2 binds to said ligands or a fragment of either ligand binds to said receptor. To practice the instant invention in a manner consistent with the breadth of the claims would not require just a repetition of the work that is described in the instant application but a substantial inventive contribution on the part of a practitioner which would involve the determination of

whether a polypeptide that comprises less than 100% of the amino acids of SEQ ID NO:2, would retain the desired activity. Furthermore, the specification does not disclose that neither the extracellular domain of SEQ ID NO:2 or a polypeptide that is at least 95% identical to SEQ ID NO:2 bind to the desired ligands. The art teaches that chemokine recognition and activation sites are distinct for each receptor. Fernandez et al teaches that mutagenesis of chemokine receptors indicates that binding sites are spread through the polypeptide, for example, CXCR4 interaction and activation with SDF-1α results from the N-terminus and ECL2 (*see Fernandez et al, Annual Review of Pharmacology and Toxicology, 2002, Vol. 42, pages 469-499, especially page 480*). Thus, the specification does not disclose that for the CCX-CKR2 polypeptide of the instant invention that the extracellular domain alone is sufficient for binding. Thus, the skilled artisan has to figure out which fragments of the polypeptide of SEQ ID NO:2 would retain the desired activity. Likewise, the artisan has to figure out whether a polypeptide that shares at least 95% identity the extracellular domain of SEQ ID NO:2 would also retain the desired activity. It is this additional characterization of the disclosed protein that is required in order to obtain the functional and structural data needed to permit one to practice the claimed method. The criteria set forth in Ex parte Forman (230 USPQ 546 (Bd. Pat. App. & Int. 1986), and reiterated in In re Wands (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)), which include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or

unpredictability of the art and (8) the breadth of the claims, is the basis for determining undue extermination. In the instant case, the quantity of experimentation to determine which of the enormous number of fragments encompassed by the claims would retain the desired activity, would be undue. Therefore, absent factual evidence, a percentage sequence similarity of less than 100% is not deemed to reasonably support to one skilled in the art whether the biochemical activity of the claimed subject matter would be the same as that of such a similar known biomolecule. It is known for nucleic acids as well as proteins, for example, that even a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many instances, albeit not in all cases. The effects of these changes are largely unpredictable as to which ones have a significant effect versus not. Therefore, the citation of sequence similarity results in an unpredictable and therefore unreliable correspondence between the claimed biomolecule and the indicated similar biomolecule of known function and therefore lacks support regarding enablement. Several publications document this unpredictability of the relationship between sequence and function, albeit that certain specific sequences may be found to be conserved over biomolecules of related function upon a significant amount of further research (see Wells, 1990, Biochemistry 29:8509-8517). Regarding

Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the sequence which are tolerant to change (e.g. such as by substitutions or deletions), and the nature and extent of changes that can be made in these positions. Reasonable correlation must exist between the scope of the

claims and scope of enablement set forth. Without sufficient guidance, the changes which can be made in the structure and still maintain sufficient activity is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue.

Therefore, the instant specification is only enabling for a method of identifying an agent that binds to the CCX-CKR2 of SEQ ID NO:2, by contacting a plurality of agents to said polypeptide and selecting an agent that competes with I-TAC or SDF1 for binding to the said CCX-CKR2 polypeptide.

Claim rejections-35 USC § 112, second Paragraph:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-10 and 28-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5a. Claim 1 in lines 4-5, it recites ", or a SDF1 or I-TAC binding fragment", which renders the claim indefinite, because it is unclear whether the a SDF1 or I-TAC needs to be present when the agent is contacted with receptor, or whether the agent is contacted with either SDF1 or I-TAC or CCX-CKR2 polypeptide. If the agent is contacted with the receptor alone, it is unclear how said agent would compete with SDF1 or I-TAC. Furthermore, the metes and bounds of "fragment" recited in claims 1 and 28 is unclear, how big is said fragment?

5b. Claim 28 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: The claim does not recite any method steps for the claimed method. The claim does not recite whether SDF-1 or I-TAC lgands are also present when the cell expressing CCX-CKR2 polypeptide comprising the extracellular domain of SEQ ID NO:2 is contacted with an agent. It is also unclear what the difference in scope between claim 1 and claim 28.

Claims 2-10 and 29-32 are rejected in so far as they depend on claims 1 and 28 for the limitations set forth above.

Conclusion:

6. No claim is allowed. The claims are free of the prior of record. As the instant specification discloses, the human CCX-CKR2 was disclosed by Sreedharan et al (1991), (see specification page 7, lines 25-33). There is a single amino acid difference between the Sreedharan et al polypeptide and the polypeptide of SEQ ID NO:2 at position 130. Sreedharan et al identified his polypeptide as being a receptor for vasoactive intestinal peptide, and named it RDC1. However, the instant specification did extensive work showing that the polypeptide of SEQ ID NO:2 is expressed in certain cancer tissues and that it binds to SDF-1 and I-TAC. Accordingly the claimed method is free of art.

Advisory Information:

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fozia M. Hamud whose telephone number is (571) 272-

0884. The examiner can normally be reached on Monday, Thursday-Friday, 6:00 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda G. Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Fozia Hamud
Patent Examiner
Art Unit 1647
18 June 2006

Eileen B. O'Hara

EILEEN B. O'HARA
PRIMARY EXAMINER